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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/931,732	08/16/2001	Bob D. Brown	OASBIO.001C1	4615

20995 7590 05/17/2005

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EXAMINER	
ASHEN, JON BENJAMIN	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 05/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/931,732	BROWN ET AL.	
	Examiner	Art Unit	
	Jon B. Ashen	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *22 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *13-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 20-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

1. Claims 1-22 are pending. Claims 13-19 were withdrawn, in the prior Office Action, from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 20-22 were newly added by Applicant in the communication filed 2/22/05. Claims 1-12 and 20-22 are currently under examination.

Applicant's response filed 02/22/2005 has been fully considered. Rejections and/or objections not reiterated from the previous office action mailed 10/20/2004 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-12 and 20-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 3, 5, 7, 9, and 11 each recite the limitation "said degenerate or universal base" in lines 4, 5 or 6. However, there is insufficient antecedent basis for this limitation in these claims. In the instant case, because the language of claims 1, 3, 5, 7, 9 and 11 preceding the above limitation recites "wherein at least one of said bases are universal and/or degenerate bases," the particular universal or degenerate base that is being referred to in "said degenerate or universal base" cannot be determined since the claimed oligonucleotide can comprise multiple mismatches. Claims 4, 6, 8, 10, 12 and 20-22 are rejected due to their dependence on a rejected claim.

4. Claims 1-12 and 20-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 3, 5, 7, 9 and 11 each recite the limitation "said nucleotide mismatch" in the last line of each claim. There is insufficient antecedent basis for this limitation in these claims. In the instant case, because the language of each claim preceding the abovementioned limitation recites "at least one nucleotide mismatch," the particular nucleotide mismatch being referred to in "said nucleotide mismatch" cannot be determined since the claimed oligonucleotide can comprise multiple mismatches. Claims 2, 4, 6, 8, 10, 12 and 20-22 are rejected due to their dependence on a rejected claim.

5. Claims 1-12 and 20-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the instant case, claims 1, 3, 5, 7, 9 and 11 each recite, "wherein said antisense oligonucleotide hybridizes to at least two RNA molecules that differ in sequence by at least one nucleotide mismatch and wherein said degenerate or universal base of said antisense oligonucleotide is positioned on said antisense oligonucleotide to correspond to said nucleotide mismatch." However, this claim language is unclear for the following reasons: As written, this claim reads on any antisense oligonucleotide that hybridizes to any two RNA molecules that can have significantly different primary nucleotide sequences as long as the two RNA molecules differ in sequence by at least one nucleotide because these two RNA molecules will differ in sequence by at least one nucleotide mismatch. The "at least one nucleotide mismatch" referred to is not required by the claim language to be in the portion of the mRNA that is hybridized by the instantly claimed antisense oligonucleotide. The claim as written, however, requires that the degenerate or universal base positioned in the antisense oligonucleotide "correspond" with "said nucleotide mismatch." Therefore, it is unclear how a universal or degenerate base, which is required to be positioned within the instantly claimed antisense oligonucleotide, can "correspond" with "said nucleotide mismatch" wherein the nucleotide mismatch (or mismatches) referred to can all be located outside the region hybridized by the antisense oligonucleotide. The metes and bounds of what is being claimed cannot be determined, rendering claims 1, 3, 5, 7, 9

and 11 indefinite. Claims 2, 4,6, 8, 10, 12 and 20-22 are rejected due to their dependence on a rejected claim.

6. Claims 1-12 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement as set forth in the Office Action mailed 10/20/2004.

Response to Arguments

7. Applicant's arguments filed 2/22/05 have been fully considered but they are not persuasive. Applicant has amended all claims and argued, on pg. 6, that the antisense oligonucleotides of the instant invention, as now claimed, have support in the specification as filed and are an important advancement over the prior art. Applicant has pointed to sequences of claimed antisense molecules that are found throughout the specification (for example pgs. 9-10 and the generic structures disclosed therein). Applicant has additionally pointed to Example 3, which describes an antisense oligonucleotide against PKCα, Example 4, which describes an antisense oligonucleotide directed to a Bcl2 target and Example 8 which describes 3 additional antisense against bcl-2. Additionally, Applicant has pointed to figures 1-3 as providing further examples of oligonucleotides that bind to different bcl or PKC targets. Applicant has asserted that each of the aforementioned 43 antisense oligonucleotides hybridize to at least two RNA molecules that differ in sequence by at least one nucleotide mismatch and at least one degenerate or universal base in each of these antisense oligonucleotides is positioned

to correspond to a nucleotide mismatch on the RNA target such that the antisense oligonucleotides can bind to the two RNAS (pg. 7, 1st full paragraph). Applicants thereby conclude that the disclosure of 46 examples of the claimed antisense by sequence, and therefore structure, satisfies the precise definition requirements of *Univ. of Rochester* and that these examples are more than sufficient to satisfy the "representative number to satisfy a genus" requirement set forth in *Eli Lilly & Co.*

However, contrary to Applicants assertions, the basis of the outstanding rejection under 35 U.S.C. § 112 1st paragraph, written description, considers that Applicant has not reasonably conveyed to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention because the specification does not provide or point to a specific structure that corresponds with the function of being antisense against at least two RNA molecules of different sequence, as claimed. Applicant, in their instant response, has pointed to generic structures of antisense oligonucleotides of their invention, but has not addressed the grounds of rejection which considers that the structures disclosed by Applicant are not correlated with the function of being antisense, as claimed. Applicant has provided examples of gene sequences known in the art to comprise nucleotide mismatches due to mutation and asserted that antisense oligonucleotides that are targeted to these regions will function as antisense. Applicant has provided no evidence of this antisense function for any of their disclosed oligonucleotides and no evidence that they were in possession of a particular antisense oligonucleotide that has the broadly claimed function of hybridizing to any two RNA molecules that differ by at least one nucleotide mismatch

(which reads on a single antisense oligonucleotide that will hybridize to any 2 RNA molecules of completely unrelated primary nucleotide sequence) and functioning as antisense.

Therefore, Applicant has not provided adequate written description of their invention because Applicant has not provided a correlation between the structure of the vast genus of antisense oligonucleotides now claimed and the function of being an antisense oligonucleotide that will modulate the expression of any two RNA molecules that differ by at least one nucleotide mismatch (which reads on every polyadenylated RNA transcript, for example). In the instant case, no structure of any particular antisense oligonucleotide, that will hybridize to any two RNA molecules that differ by at least one nucleotide mismatch, is provided that corresponds with the function of being an antisense oligonucleotide that modulates the expression of both RNAs, that would indicate that Applicant was in possession of the instant invention commensurate with the breadth of the what is claimed, which is a genus of antisense oligonucleotides that will modulate the expression of any two RNA molecules that can have vastly different primary nucleotide sequences.

Claim Rejections - 35 USC § 102

8. The following interpretation of the instant claim language was set forth, for the purposes of clarification, in the prior Office Action and is reiterated herein. In the instant case, the specification as filed indicates that a universal base refers to a moiety that may be substituted for any base, that need not contribute to hybridization but that

should not significantly detract from hybridization (pg. 6, specification as filed). The particular meaning of "significantly detract" is not set forth. As interpreted herein, a universal base according to Applicant's definition, encompasses any moiety that can be substituted for any base as long as it does not significantly detract from hybridization and therefore, includes, at least, other modified and non modified nucleobases (as these would not significantly detract from hybridization). In light of this, a reasonable interpretation of the claim language, "wherein said antisense oligonucleotide hybridizes to at least two RNA molecules that differ in sequence by at least one nucleotide mismatch and wherein said degenerate or universal base of said antisense oligonucleotide is positioned on said antisense oligonucleotide to correspond to said nucleotide mismatch" reads on any antisense oligonucleotide that hybridizes to any two RNA molecules that can be of significantly different primary nucleotide sequence, as long as sufficient primary nucleotide sequence identity in some region is shared such that an antisense oligonucleotide will hybridize to both RNAs (e.g., transcriptional splice variants, homologous mRNAs from different organisms etc., 16s rRNA from any two bacteria, histone mRNA from any two eukaryotes, etc.). These two RNA molecules will differ in sequence by at least one nucleotide mismatch (because nucleotide mismatches are not required by the claim language to be positioned within the region of the two RNA molecules that is bound by the instantly claimed antisense oligonucleotide) and the position of any "universal" bases in the antisense oligonucleotide itself will correspond to the at least one nucleotide mismatch on both RNA molecules in that it will be in the same relative and fixed position within the oligonucleotide. In regards to "RNA targeting

region," no definition of what is intended by this phrase is provided in the specification as filed. Therefore, any region of any oligonucleotide that has the potential to bind to any RNA is considered to be an RNA targeting region. In light of the above interpretations, the following art is applied.

9. Claims 1-8 remain rejected and 20-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Cook et al. (U.S. Patent 5,623,065) as set forth in the Office Action mailed 10/20/2004 and reiterated herein. Claims 1-8 are drawn to an antisense oligonucleotide that comprises at least one non-naturally occurring backbone linkage that comprises at least one universal and/or degenerate base, that is between 6 and about 50 bases (claim 1), an antisense oligonucleotide that comprises a first and second non-RNase H recruiting region of between 3 and about 15 bases, an RNase H recruiting region of between 3 and about 15 bases, and a second RNase H recruiting region wherein at least one base is a universal and/or degenerate base (claim 3), an antisense oligonucleotide that comprises a non-RNase H recruiting section and an RNase H recruiting section wherein at least one base is a universal and/or degenerate base (claim 5) and an antisense oligonucleotide that comprises an RNase L recruiting region comprising a 2'-5' adenosine oligomer wherein an RNA targeting region of said antisense oligonucleotide comprises at least one universal and/or degenerate base (claim 7). The antisense oligonucleotides of claims 1, 3, 5 and 7 can have no more than about 50% universal and/or degenerate bases (claims 2, 4, 6 and 8 that depend from claims 1, 3, 5 and 7 respectively). Each of the oligonucleotides of the instant invention

claimed in claims 1, 3, 5 and 7 is an antisense oligonucleotide that complements at least two RNA molecules of different structure.

Cook et al. disclose antisense phosphorothioate oligonucleotides that are 17 bases in length (columns 25-26, table 1) that comprise 2'-O-methyl modified sugars of 4-7 bases that flank, on both the 3' and 5' ends, between 3 and 9, 2'-deoxy-erythro-pentofuranosyl nucleotides (SEQ ID NOS: 3-6 in table 1) that are antisense oligonucleotides targeted to the codon 12 point mutation of activated H-ras that comprise at least 1 non-naturally occurring backbone linkage, are between 6 and about 50 bases, that further comprise RNase H recruiting and non-RNase H recruiting regions and sections that further comprise sequence motifs with one or more universal bases (because "universal bases" can be any bases) wherein the sequence motifs are "cg" or poly-g ("gg"), as claimed. Cook et al. also disclose the preparation of a 20mer oligonucleotide that comprises a 1st region of 6, 2'-5' linked RNA that is attached to a 2'-deoxy phosphorothioate region of 3'-5' linked DNA 8 nucleotides long and a further 6 nucleotide long region of 2'-5' linkages that are added to complete an oligonucleotide having mixed 2'-5' and 3'-5' linkages. In this embodiment, the prior art antisense oligonucleotide of Cook et al. comprises an RNase L recruiting region (that can be 6, 2'-5' linked RNA nucleotides that can be adenosine) and a non-RNase L recruiting region. Any of the prior art antisense oligonucleotides of Cook et al. can comprise a universal base, for example xanthine (column 5, line 62), which is disclosed without limitation, and can therefore be positioned in the RNA targeting region of an antisense oligonucleotide and used to construct an antisense oligonucleotide comprising no more

than about 50% universal and/or degenerate bases. Moreover, based on a reasonable interpretation of "universal" base as set forth above in this rejection, the prior art antisense oligonucleotides of Cook et al., will hybridize to two RNA molecules of different sequence in that they are complements of wild type (codon 12 = ggc) and mutant, activated, H-ras (codon 12 = gtc), wherein the universal base that corresponds to the nucleotide mismatch is the "A" base that hybridizes to the mutant "t" in the h-ras codon 12. Therefore, Cook et al. anticipate the instant invention as set forth in claims 1-8.

10. Claims 1, 2 and 4-8 remain rejected and claims 20-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Torrence et al. (U.S. Patent 5, 583, 032), as set forth in the Office Action mailed 10/20/2004 and reiterated herein. The invention claimed in claims 1, 2 and 4-8 is set forth in a previous rejection. Torrence et al. disclose a chimeric antisense oligonucleotide that targets PKR mRNA at positions 55-73 from the start codon of the PKR mRNA (SEQ ID NO: 6) that comprises 4, 2'-5' linked adenosines (an RNase L-recruiting region) and an a 3',5' –deoxyribonucleotide antisense sequence (an RNA targeting region) (column 24, example 7). Torrance et al. disclose that possible antisense moiety constituents can include alpha-deoxynucleotides (universal bases according to Applicant's definition on page 6 of the specification as filed) (column 5, line 61). No limitations are disclosed in regards to the possible antisense moiety constituents of Torrence et al., which can be positioned in the RNA targeting region of an antisense oligonucleotide and used to construct an

antisense oligonucleotide comprising no more than about 50% universal and/or degenerate bases. The prior art antisense oligonucleotide of Torrence et al. will hybridize to at least two RNA molecules that differ in sequence by at least one mismatch because it will hybridize, at least, to both mouse and human PKR mRNA. The terminal 4, 2'-5' linked adenosines of the antisense oligonucleotide of Torrence et al. are also considered universal or degenerate bases as per Applicant's disclosure in the specification, because they do not significantly detract from hybridization. In being located on the end of the antisense oligonucleotide of Torrence et al., these adenosine bases correspond with the same nucleotide mismatches on both the mouse and human PKR mRNAs. In light of the 112 2nd paragraph rejection of claims 21 and 22 set forth previously in this Action and a reasonable interpretation of universal and/or degenerate base (based on the disclosure of the specification and as also set forth previously in this Action), the antisense oligonucleotide of Torrence et al. comprises one or more sequence motifs with one or more degenerate and or universal base wherein said motif is a "CG" or a poly-G. Therefore, Torrence et al. anticipate the instantly claimed invention as set forth in claims 1, 2 and 4-8.

11. Claims 1, 2, 7, 8, 11 and 12 remain rejected and claims 20-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Stinchcomb et al. (U.S. Patent 5,646,042), as set forth in the Office Action mailed 10/20/2004 and reiterated herein. The invention claimed in claims 1-2 and 7-8 is set forth in a previous rejection. Claims 11 and 12 are drawn to a ribozyme comprising an RNA targeting region which comprises at least one

universal and/or degenerate bases that hybridizes to at least two RNA molecules of a different sequence (claim 12) wherein said RNA targeting region comprises no more than about 50% universal and/or degenerate bases. Stinchcomb et al. disclose an antisense oligonucleotide that is an optimal c-myb hammerhead ribozyme that comprises phosphorothioate linkages at the 5' end, that is 37 bases in length, that comprises a 3'-3' abasic deoxyribose (3'-3' linked inverted T) and a 2'-C-allyl U, each of which are considered a universal base as per Applicant's definition on page 6 of the instant specification, wherein said universal bases comprise no more than about 50% of the RNA targeting region (Fig. 20, brief description of the drawings and Example 14 (at least). The prior art anti-c-myb ribozymes of Stinchcomb et al. are disclosed as active against both human and murine mRNA transcripts (column 14, lines 33-41), which indicates that they hybridize to at least two RNA molecules of a different sequence. Stinchcomb et al. also disclose a ribozyme that targets c-myb site 575 (one of the several ribozymes disclosed that target both human and murine mRNA molecules) that is synthesized with 2-5A moieties at the 5' end (575 active Rz + active P(A)4) (column 28, lines 1-25). The terminal 2-5A moieties of the ribozyme of Stinchcomb et al. are also considered universal or degenerate bases as per Applicant's disclosure in the specification, because they do not significantly detract from hybridization. In being located on the end of the ribozyme of Stinchcomb et al., these adenosine bases correspond with the same nucleotide mismatches on both the human and murine c-myb mRNA transcripts. Additionally, the 3' abasic deoxyribose (3'-3' linked inverted T) and a 2'-C-allyl U disclosed by Stinchcomb et al. maintain the same absolute position in the

ribozyme that targets both human and murine transcripts. In the instant case, the mismatches required to meet the claim limitations are located on either side of the nucleotide sequences recognized by the ribozyme binding arms. In this regard, the universal and/or degenerate bases disclosed by Stinchcomb et al. correspond to the same nucleotide mismatches of the human and murine mRNA transcripts. The 575 ribozyme of Stinchcomb et al. comprises one or more sequence motifs with one or more degenerate and/or universal bases wherein said motif is a "CG" or a poly-G (col. 33, Table 3). Therefore, Stinchcomb et al. anticipate the instant invention as set forth in claims 1, 2, 7, 8, 11 and 12.

12. Claims 1-6 remain rejected and claims 20-22 are rejected under 35 U.S.C. 102(e) as being anticipated by Bennett et al. (U.S. Patent 6,172,216), as set forth in the Office Action mailed 10/20/2004 and reiterated herein. . The invention as set forth in claims 1-6 is described in a previous rejection. Bennett et al. disclose SEQ ID NO: 31, an antisense oligonucleotide targeted to mRNA transcripts of both human bcl-xl and bcl-xs that is a chimeric oligonucleotide "gapmer" that is 20 nucleotides in length and composed of a central gap region consisting of ten 2'-deoxynucleotides which is flanked on both sides by 5 nucleotide wings composed of 2'-0-methoxyethyl nucleotides (a first and second non-RNase H recruiting region that are the 2'-MOE wings and an RNase H recruiting region that is the region of ten 2'-deoxynucleotides) (col. 35, Table 8). The internucleoside linkages are phosphorothioate throughout. Four cytidine residues (out of a total of 20 residues in the oligonucleotide) in the 2'-MOE

wings are universal bases that are 5-methylcytidine (column 28, example 18). The antisense oligonucleotide of Bennett et al. hybridizes to at least two RNA molecules that differ in sequence by at least one nucleotide mismatch. The universal bases comprised in the antisense oligonucleotide of Bennett et al. are fixed in position and will correspond, whether the antisense oligonucleotide of Bennett et al. is hybridized to the bcl-xs or bcl-xl transcript, to the same nucleotide mismatches. In light of the 112 2nd paragraph rejection of claims 21 and 22 set forth previously in this Action and a reasonable interpretation of universal and/or degenerate base (based on the disclosure of the specification and as also set forth previously in this Action), the antisense oligonucleotide of Bennett et al. comprises one or more sequence motifs with one or more degenerate and or universal base wherein said motif is a "CG" or a poly-G. Therefore, Bennett et al. anticipate the instant invention as set forth in claims 1-6 and 20-22.

13. Applicant's arguments filed 2/22/2005 have been fully considered but they are not persuasive. Applicant has amended instant claims 1, 3, 5, 7, 9 and 11 argued, in regards to the outstanding rejections of claims 1-8 under 35 U.S.C. 102(b) as being anticipated by Cook et al. (U.S. Patent 5,623,065), claims 1, 2 and 4-8 under 35 U.S.C. 102(b) as being anticipated by Torrence et al. (U.S. Patent 5, 583, 032), claims 1, 2, 7, 8, 11 and 12 under 35 U.S.C. 102(b) as being anticipated by Stinchcomb et al. (U.S. Patent 5,646,042) and claims 1-6 under 35 U.S.C. 102(e) as being anticipated by Bennett et al. (U.S. Patent 6,172,216), that the now pending claims recite antisense

oligonucleotides and ribozymes that hybridize to at least two RNA molecules that differ in sequence by at least one nucleotide mismatch, and wherein a degenerate or universal base is positioned on said oligonucleotide or ribozyme to correspond to said nucleotide mismatch. As Cook et al., Torrence et al., Stinchcomb et al. and Bennett et al. do not teach an antisense oligonucleotide having a degenerate or universal base positioned to correspond to a nucleotide mismatch on a target sequence, Applicants respectfully request the withdrawal of this rejection (pg. 8, 1st thru 3rd full paragraphs; pg. 9, 1st full paragraph). However, contrary to Applicant's arguments, the instant claim language is not so limiting as to exclude the prior art of Cook et al., Torrence et al., Stinchcomb et al. and Bennett et al. as applied above (as set forth in previous rejections herein). Therefore, Cook et al., Torrence et al., Stinchcomb et al. and Bennett et al. still anticipate the instant invention as set forth in claims 1-8 and 20-22.

Claim Rejections - 35 USC § 103

14. Claim 7-12 are maintained as rejected under 35 U.S.C. 103(a) as being unpatentable over Werther et al. (U.S. Patent 5,929,040) in view of Bennett et al. (U.S. Patent 6,172,216), Torrance et al. (U.S. Patent 5,583,032) and Krupp (1993, reference 82, PTO-1449 filed 8/28/02) for the reasons of record as set forth in the prior Office Action.

Response to Arguments

15. Applicant's arguments filed 2/22/05 have been fully considered but they are not persuasive. Applicant has argued that the cited art fails to teach or suggest all of the

claim limitations because the claims have been amended to recite antisense oligonucleotides and ribozymes that hybridize to at least two RNA molecules that differ in sequence by at least one nucleotide mismatch, and wherein a degenerate or universal base is positioned on said oligonucleotide or ribozyme to correspond to said nucleotide mismatch. Applicant has therefore argued that the cited references alone or in combination do not teach, suggest, or motivate one of skill in the art to make an antisense oligonucleotide or ribozyme having a degenerate or universal base positioned to correspond to a nucleotide mismatch on a target sequence. However, contrary to Applicants argument, and as set forth previously in this Action, the instant claim language is not so limiting as to exclude the cited prior art of Torrence et al. and Bennett et al., whose teachings that are relied upon, in combination with Werther et al. and Krupp et al., in the outstanding rejection under 35 U.S.C. § 103(a). Therefore, the cited prior art, taken as a whole and as set forth in the Office Action mailed 10/20/2004, teaches, suggests and motivates the instant invention set forth in claims 7-12.

Conclusion

16. No claims are allowed.

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon B. Ashen whose telephone number is 571-272-2913. The examiner can normally be reached on 7:30 am - 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Jba

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